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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,568	07/30/2001	Wataru Morikawa	20-48418	2810

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EXAMINER

HARRIS, ALANA M

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 05/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/806,568

Applicant(s)

MORIKAWA ET AL.

Examiner

Alana M. Harris, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 February 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 and 13-17 is/are pending in the application.
- 4a) Of the above claim(s) 5-10, 13 and 14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 11 and 15-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Arguments and Amendments

1. Claims 1-11 and 13-17 are pending.

Claims 5-10, 13 and 14, drawn to non-elected inventions are withdrawn from examination.

Claim 2 has been amended.

Claims 1-4, 11 and 15-17 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Rejection

Claim Rejections - 35 USC § 112

3. The rejection of claim 17 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in light of Applicants' response and guidance within the specification.

4. The rejection of claims 2, 3 and 15 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Claim Rejections - 35 USC § 102

5. The rejection of claims 1-4, 11 and 15-17 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent number 5,800,814 (filed April 22, 1994) is withdrawn in light of Applicants' arguments submitted February 17, 2005.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

6. Claims 1-4, 11 and 15-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims broadly state an aspartic enzyme that produces plasma protein fragments having an inhibitory activity of metastasis and growth of cancer. As the claims read this claimed product is not isolated, nor described by any particular structure. Applicants have listed that the N-terminus of the enzyme has ten specific amino acid residues, SEQ ID NO: 1, however there is no information regarding the remaining residues, i.e. carboxy terminus. And while it is clear that the claimed product is to function as an enzyme which facilitates cleavage of plasminogen and fibronectin into fragments, which are able to exert an inhibitory activity of metastasis and growth of cancer there is no corresponding structure, see specification, page 1, lines 10-15. Applicants have not provided sufficient evidence that they were in possession of the

wide breadth of proteins that could be regarded as an aspartic enzyme able to produce protein fragments. The simple statement of function for the claimed protein does not full the written description requirement.

It is established in this instant case Applicants seem to be in possession of an aspartic enzyme included within the PC-3 culture supernatant designated by Applicants as plasminogen angiostatin converting enzyme of pH 4 (PACE4), see page 9, lines 19-24 and page 19, lines 2-6. However, this is insufficient description providing evidence Applicants are in possession of a genus of aspartic enzymes, which are not defined by structure. The little information given regarding the amino acid sequence is insufficient in evidencing a correlation between function and structure. Functional characteristics when coupled with a known or disclosed correlation between function and structure or some combination of such characteristics are evidence that Applicants' invention is complete and Applicants were in possession of the claimed invention. The written description is not commensurate in scope with the claims drawn to an enzyme simply characterized solely by function.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC

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112 is severable from its enablement provision (see page 115).

Applicants are not entitled, nor does the specification evidence the possession of all aspartic enzymes that produce plasma protein fragments. Applicants are not permitted to claim the enumerable proteins simply referenced as aspartic enzymes that degrade or produce plasma proteins and have a N-terminal amino acid sequence of LVRIPLHKFT (SEQ ID NO: 1). Accordingly, Applicants are not entitled to the wide breadth of the claims at issue.

This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Claim Rejections - 35 USC § 102

7. The rejection of claims 1-4, 11 and 15-17 under 35 U.S.C. 102(b) as being anticipated by Gately et al. (Cancer Research 56: 4887-4890, November 1, 1996/ IDS reference on sheet 1) is reinstated and newly made. Applicants argued and submitted a declaration on July 22, 2004 in response to the rejection set forth in the Action mailed March 1, 2004. However, upon reconsideration the instant rejection is established.

Applicants have fervently argued that the enzyme of Gately is distinct from the claimed invention because of the following assertions:

(a) the enzymatic activity of Gately's protein is inhibited by a serine proteinase inhibitor as opposed to the aspartate proteinase inhibition of the claimed protein, see page 6, lines 10-33 of the declaration; and

(b) the enzyme of Gately is a serine protease acting at a neutral pH range in contrast to the enzyme of the present invention, an aspartate protease acting at an acidic pH range, see page 7, lines 3-8 of declaration.

These points of view and arguments have been carefully considered, but found unpersuasive.

Gately discloses a factor secreted by several prostate carcinoma cell lines including the PC-3 cell line that has enzymatic activity and is able to cleave plasminogen to bioactive angiostatin, see page 4887, abstract and introduction. Applicants have noted that their enzyme was "...prepared in accordance with Gately et al.", see page 14, lines 9-11. The factor identified by Gately inherently comprised Applicants' claimed enzyme. The enzyme activity contained in Gately's factor exerts the same activity as Applicants' claimed enzyme. Applicants have noted on the record that the plasminogen angiostatin converting enzyme (PACE) of Gately was not isolated and established, see page 14, lines 6-11. However, the supernatant containing the enzyme was separated from the cell culture source thereby inherently isolated from the said source. Notwithstanding, Gately's factor derived from PC-3 would in fact contain the claimed enzyme. Unless the PC-3 cells of Gately were different from the PC-3 cells of Applicants the disclosed enzyme is one in the same as Applicants.

It is reasonable to conclude that given the starting material of Gately is the same as Applicants the disclosed enzyme reads on Applicants and inherently cleaves plasminogen at 73L-74F and/or 451L-452P, is active at a pH of not more than 5.0, inhibited by an aspartic protease inhibitor and has the N-terminal amino acid sequence

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of SEQ ID NO: 1. While Gately seemingly did not perform the proteinase inhibitor assay at the same pH as Applicants this does not teach away from the simple fact that enzyme of Gately contained in the PC-3 supernatant is the enzyme of Applicants.

Based on the analysis set forth in the preceding paragraphs including factual and technical grounds provided by the prior art the inherent features necessarily flow from the said art and the rejection stands.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The examiner works a flexible schedule, however she can normally be reached between the hours of 6:30 am to 5:30 pm with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.

PRIMARY EXAMINER



Alana M. Harris, Ph.D.

12 May 2005